Remarks

Claims 1-7 are pending.

By the above amendment, independent claims 1, 5, and 7 have been rewritten in a manner to more clearly follow antecedent terminology. Claims 1 and 5 have also been amended to more clearly define the characteristic of the transgenic mouse as having insensitivity to amnesic effects of scopolamine as demonstrable in a passive avoidance test, as supported in the specification, e.g., at pages 10 and 17-18.

In the outstanding Office Action, the Examiner rejected original claims 2-5 under 35 U.S.C. § 112, second paragraph, as being indefinite. In particular, the Examiner pointed out that: each recitation of "the . . . gene" in original claims 2-4 lacked precise antecedent basis; the recitation of "a mouse blastocysts" in original claim 5 was grammatically incorrect; and the recitation of "the blastocysts" in claim 5 lacked precise antecedent basis. The noted informalities have been corrected by the above amendment. Accordingly, the rejection under the second paragraph of Section 112 has been overcome.

The Examiner also rejected claims 1-7 under 35 U.S.C. § 101 as lacking utility and 35 U.S.C. § 112, first paragraph, as lacking an enabling description of how to use the claimed invention. Both rejections are grounded on the supposed lack of any teaching in the specification of how to use mice that are resistant to the amnesic effects of scopolamine. These rejections are respectfully traversed.

In the utility and enablement rejections, the Examiner stated:

> "The specification teaches H3-/- mice are resistant to the amnesic effect of scopolamine. . . . The specification does not teach how to use mice that are resistant to the amnesic effect of scopolamine. The art at the time of filing did not teach how to use such a mouse. . . . [W]hile the phenotype of the mouse is specific, the function of H3 receptors in the role of the amnesic effect of scopolamine is not. The insensitivity to scopolamine implies H3 receptors merely play a role in "passive avoidance." It remains unknown how H3 receptors function in the amnesic effect of scopolamine.

Notwithstanding that all specific roles or biological functions of H3 receptors may not have been known at the time of the invention, the claimed invention has utility and is supported by an enabling disclosure of how to use the invention. Indeed, the Examiner's comments support, rather than negate, the utility of the transgenic mice of the invention--i.e., the mice are useful as research tools for studying the roles of H3 receptors, like other knockout mice are useful in general. For example, compare Masaki et al., "Targeted Disruption of Histamine H_1-Receptor Attenuates Regulatory Effects of Leptin on Feeding, Adiposity, and UCP Family in Mice," *Diabetes*, vol. 50, February 2001, 385-391 (submitted with Supplemental Information Disclosure Statement dated August 6, 2003).

Moreover, the specification provides ample guidance on the use of the claimed invention, taking into account the knowledge and level of ordinary skill in the art. For example, the specification teaches that the transgenic mice and the cells derived therefrom "provide a valuable animal model and tools to understand the function of the histamine H3 receptor and to evaluate the therapeutic effects of drugs that modulate the function or the expression of the H3 receptor equivalents in human cells" (page 2, lines 10-14). The specification also describes that the mice may be used to: "dissect the *in vivo* role of histamine H3 receptor signaling pathways" (page 2, lines 1-2);

establish "a nonhuman model for diseases involving histamine H3 receptor equivalents in the human" (page 4, lines 8-10); study the functional role of a drug target by studying "the defects resulting from the disrupted gene in a whole animal" (page 7, lines 26-27); and "allow the definition of the function of histamine H3 receptor which is critical in deciding the types of modulators . . . most suitable in therapies" (sentence bridging pages 7 and 8).

Furthermore, the specification includes examples of specific utilities of the claimed mice, which have a disruption in an endogenous histamine H3 receptor gene generated by targeted replacement with a non-functional histamine H3 receptor gene (as demonstrable by insensitivity to amnesic effects of scopolamine in a passive avoidance test). Specifically, use of the transgenic mice in passive avoidance tests to study the efficacy of experimental histamine H3 receptor antagonists or modulators is one particular utility apparent from the application (see example at pages 17-18). Another illustrative utility is for studying the effects of histamine H3 receptor antagonists on sleep-wake states (see example at page 16).

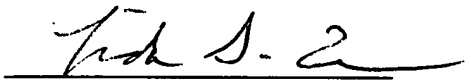
Since a person of ordinary skill in the art would readily appreciate why the invention is useful based on its characteristics, and the utility is specific, substantial, credible, and supported by an enabling disclosure, the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, are in error and should be withdrawn.

In view of the foregoing, all of the claims are allowable. Applicant therefore

requests prompt and favorable action as well as official confirmation of the Examiner's consideration of the references submitted with the Supplemental Information Disclosure Statement dated August 6, 2003.

Respectfully submitted,

Date: February 24, 2004



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